

## REMARKS

Favorable reconsideration is respectfully requested.

The claims are 11 to 14 and 16 to 23.

Claims 11 to 14, 16 to 21 and 23 stand finally rejected under 35 U.S.C. 103(a) as being unpatentable over Effenberger et al (US 4,859,784) and further in view of Collet et al and further in view of McMasters.

This rejection is respectfully traversed.

A brief discussion of the present invention will be of assistance in appreciating applicant's reasons for traversal of the rejection.

Aim of the present invention was to find a possibility of simultaneously increasing the chemical and the optical purity of  $\alpha$ -hydroxycarboxylic acids, obtained by enzyme-catalyzed addition of a cyanide group to an aldehyde or ketone with subsequent acidic hydrolysis.

The enzymatic addition of a cyanide group to an aldehyde or ketone is not the inventive step but rather state of the art as already described in the specification on page 2, lines 29 to 34.

Also the acidic hydrolysis is not the inventive step, but rather state of the art as already described in the specification on page 3, line 38 to page 4, line 6.

The present invention resides in the special recrystallization of hydroxycarboxylic acids, obtained by these two known steps, which leads to an increase in optical as well as in chemical purity of the hydroxycarboxylic acids.

Effenberger represents state of the art for the enzymatic addition of HCN to an aldehyde or ketone using D-oxynitrilase to form the corresponding cyanohydrin.

This enzymatic addition can be performed in an organic solvent, which may be saturated with water or an aqueous buffer solution.

Since this step does not correspond to the claimed inventive recrystallization step, Effenberger is not relevant, especially it is not relevant as what solvent is used for the enzymatic addition step, since this enzymatic addition step is not the present invention.

Further as explained in the Supplementary Response of May 28, 2002, water or an aqueous buffer is not a suitable co-solvent as used for recrystallization according to the present invention, since water is not (or is only slightly) miscible with the aromatic hydrocarbon and can therefore not increase the solubility of the hydroxycarboxylic acid.

As already mentioned in the previous response, it is true that Effenberger suggests that the crude nitrile solution can be directly used for the hydrolysis step in order to obtain the corresponding optically active 2-hydroxycarboxylic acid.

But this step is not the present invention, but rather the state of the art as explained above.

The crucial point of the present invention is to increase the chemical purity as well as the optical purity of the produced acids.

Collet discloses on page 3332, right column, last paragraph a process for the synthesis of **racemic** substituted mandelic acid, and not, as stated by the rejection, of optically pure acids.

Further Collet discloses the acidic hydrolysis of racemic halomandelonitriles to the corresponding racemic substituted mandelic acids, which then must be reacted with (-)-ephedrine to form the diastereomeric salts. This salt has to be decomposed with an acid, for instance with HCl, and recrystallized to yield the optically enriched respectively pure acid. **No ee-value is disclosed and no chemical purity is cited.** There is absolutely no disclosure or suggestion in the Collet reference that the chemical as well as the optical purity of already optically enriched hydroxycarboxylic acids could be increased by the special recrystallization step as claimed herein.

No art-skilled person could conclude from the Collet reference that recrystallization would have the effect of improving the optical purity as well as the chemical purity of the desired optically active hydroxycarboxylic acids, since there is absolutely no suggestion in the Collet reference that a single recrystallization step, as presently claimed, could improve the optical purity as well as the chemical one.

Further there is absolutely no suggestion in the Collet reference that the recrystallization (in order to improve the chemical and the optical purity) could be carried out in the hydrolysis medium as is claimed herein (claim 16).

Further the process according to Pöchlauer is also not obvious over the combined references (Effenberger and Collet), since first of all none of these references suggests or discloses that the optical and chemical purity of hydroxycarboxylic acids, obtained by acidic hydrolysis of optically active nitriles, could be improved by a single recrystallization step using aromatic hydrocarbons, optionally with a co-solvent and none of them discloses and suggests that the hydrolysis solution obtained by acidic hydrolysis can be treated directly with aromatic hydrocarbons, optionally with a co-solvent as claimed in claim 16.

McMasters teaches a conventional recrystallization process, but McMasters does not disclose or suggest in any way that the special recrystallization as claimed herein could increase the chemical as well as the optical purity of already optically enriched hydroxycarboxylic acids.

On page 2, 2<sup>nd</sup> paragraph, McMasters discloses that if no single solvent is found suitable, then a mixed solvent recrystallization is in order.

According to the present method, however, the claimed solvents are also suitable to increase the chemical as well as the optical purity of already optically enriched hydroxycarboxylic acids if used single.

Further McMasters discloses that for mixed solvent recrystallization, the substance should be relatively soluble in one solvent and relatively insoluble in another solvent. This is not true for the cosolvents used herein.

The hydroxycarboxylic acids are also relatively soluble in the cosolvents used herein, therefore they are used to increase the solubility of the acids in the organic phase, as disclosed in the specification on page 4, lines 18 to 20.

The addition of the cosolvent herein has further the advantage that the optical purity can be further increased compared to the use of a single solvent, as can be seen from Example 3.

All of these aspects are neither disclosed nor suggested by the McMasters reference.

Summing up, from the facts discussed above, the presently claimed special recrystallization step could not have been obvious to an art-skilled person, since firstly Effenberger only discloses the enzymatic addition step and the hydrolysis step, which are not the invention herein; secondly there is absolutely no disclosure or suggestion in the Collet reference

that the chemical as well as the optical purity of already optically enriched hydroxycarboxylic acids could be increased by the special recrystallization step as claimed herein and further also McMasters neither discloses nor suggests that the chemical as well as the optical purity of already optically enriched hydroxycarboxylic acids could be increased by the special recrystallization step as claimed herein.

Further there is absolutely no suggestion in any of the references that the recrystallization (in order to improve the chemical and the optical purity) could be carried out in the hydrolysis medium as is claimed herein.

Claim 22 stands rejected under 35 U.S.C. 103(a) as being unpatentable over Effenberger et al and Collet et al and McMasters as applied to claims 11 to 14, 16 to 21 and 23 above, and further in view of Bryker et al (US 4,983,771).

This rejection is respectfully traversed.

Bryker discloses that mandelic acid, which is used as resolving agent for recovering optically pure phenylethylamine, can be recovered from the reaction mixture by extracting with MIBK.

There is absolutely no suggestion or disclosure that the optical purity of already optically enriched hydroxycarboxylic acids could be increased by the special recrystallization step as claimed herein.

Further, it is apparent that Bryker cannot overcome the deficiencies of the above-discussed references.


For the foregoing reasons, it is apparent that the rejections on prior art are untenable and should be withdrawn.

No further issues remaining, allowance of this application is respectfully requested.

If the Examiner has any comments or proposals for expediting prosecution, please contact the undersigned at the telephone number below.

Respectfully submitted,

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